

Abstract

Polymer based microneedle (MN) systems are widely used for biocompatible and resorbable drug delivery. However, the spatial and temporal control of drug release has been a common problem of MN. Herein, we developed an on-demand drug release MN system based on metal encapsulation and electrochemical corrosion. Electrically triggered drug release at desired time and ultrafine spatial control of single needle was realized. This strategy can be further applied into closed-loop drug delivery systems or be integrated with Bluetooth for wireless control.

Design

Fig. 1. The schematic illustration of the MN device.

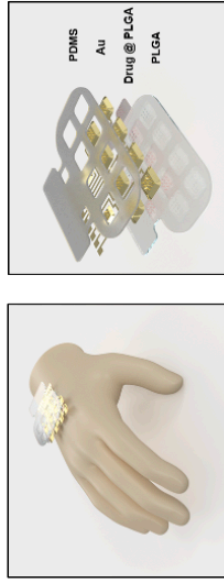
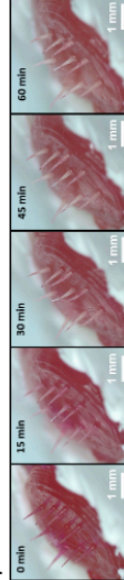


Fig. 2. The optical microscopy characterization of MN array at different degree of electrochemical corrosion (0, 0.5, and 2 min).



Fig. 3. The optical microscopy characterization of the dye release process from the initial state to 60 min.



- Wet mold casting methods were developed to yield high quality MNs and allowed for convenient drug loading at ambient temperature.
- PDMS mold can be easily designed into different shapes to meet the need of different applications.
- The negative molds on PDMS were fabricated by UV laser ablation. The length of the MN can be tuned from 0.6 – 3 mm.
- Au layer was deposited by sputter coating and patterned by IR laser ablation, which was eventually connected with wires or conductive tapes.
- Rhodamine B was used to simulate the release of small molecular and water soluble drug. The release process was carried out in standard 1x DPBS and monitored by UV-Vis spectroscopy. (Fig. 3.)

Results

Fig. 4. A. The dye release with and without Au encapsulation layer. Fig. 4. B. The step wise dye release by electrical triggering.

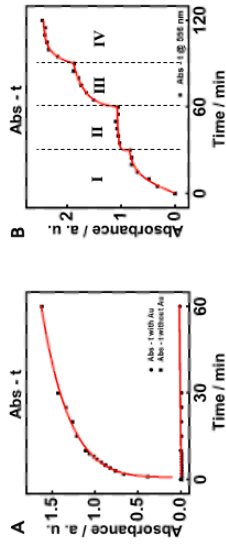


Fig. 5. The EDXS element analysis of MN at different stages.

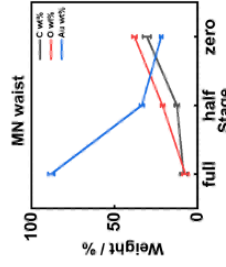


Fig. 6. The amperometry of Au corrosion at different voltages.

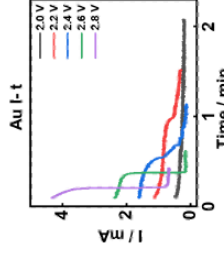
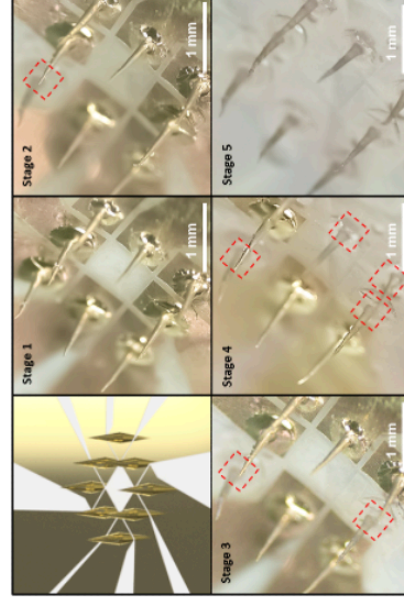


Fig. 7. The needle-wise electrochemical corrosion of an 8-needle MN array. Red squares refer to the MN triggered in the last step.



- The electrochemical corrosion of surface coating was characterized. (Fig. 2, 5, 6.)
- 100-150 nm Au layer on MN array provides enough encapsulation to prevent the early release of dye. The release kinetics was fitted by a modified Weibull function. (Fig. 4.A.)
- A four-step controlled dye release was realized by electrical trigger. (Fig. 4.B, 8.)
- The spatial resolution of the electrical triggering can be up to 1 mm². (Fig. 7.)

Results

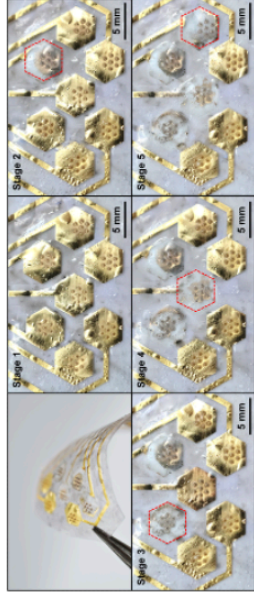


Fig. 8. The stepwise electrochemical corrosion of a multi-array MN patch.

Conclusion

- We developed an MN system to achieve high spatial and temporal control of drug delivery.
- The performance of Au encapsulation was validated, while the electrochemical corrosion of Au can be completed within 0.5 min at a rather safe potential.
- High spatial resolution of electrical triggering was realized.

Future development

- The electrical trigger can be realized wirelessly for implantable drug delivery.
- The current MN system can be integrated with biochemical sensors to realize a close-loop therapy. For example, glucose sensors can be connected to the device to realize a self-adjusted delivery of insulin or metformin, for diabetes treatment.
- The feature of high spatial and temporal resolution may benefit the study of neural interface drug delivery, which requires precise control of the dosage and position.

references

- Koo, J. et al. Wirelessly controlled, bioresorbable drug delivery device with active valves that exploit electrochemically triggered crevice corrosion. *Sci Adv.* 6, (2020).
- Mirvakili, S. M. & Langer, R. Wireless on-demand drug delivery. *Nat. Electron.* 4, 464–477 (2021)
- Huang, Y. et al. Implantable Electronic Medicine Enabled by Bioresorbable Microneedles for Wireless Electrotherapy and Drug Delivery. *Nano Lett.* (2022) doi:10.1021/acs.nanolett.2c01997.